

In the Claims

Please amend Claims 1, 7, 17, and 28. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages i - ii).

1. (Three times amended) A retroviral vector which undergoes promoter conversion comprising in 5' to 3' order,

- a) a 5' long terminal repeat region of the structure U3-R-U5;
- b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the vector; and
- c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a heterologous promoter other than a promoter from a retrovirus upon which the retroviral vector is based or a promoter from a subtype of the retrovirus upon which the retroviral vector is based is inserted, said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences.

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7. (Three times amended) The retroviral vector according to Claim 31, wherein said promoter is selected from the group consisting of: a Whey Acidic Protein specific promoter, a Mouse Mammary Tumor Virus specific promoter β -lactoglobulin and casein specific promoters, a pancreas specific promoter, lymphocyte specific promoter, a Mouse Mammary Tumor Virus specific promoter conferring responsiveness to glucocorticoid hormones or directing expression to the mammary gland, and combinations thereof.

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17. (Three times amended) A retroviral vector kit comprising:

a retroviral vector which undergoes promoter conversion comprising in 5' to 3' order, a) a 5' long terminal repeat region of the structure U3-R-U5; b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the

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body of the vector; and c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a heterologous promoter is inserted, wherein said promoter is derived from a promoter other than a promoter from a retrovirus upon which the retroviral vector is based or a promoter from a subtype of the retrovirus upon which the retroviral vector is based and said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences; and

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a packaging cell line harboring at least one retroviral or recombinant retroviral construct coding for proteins required for said retroviral vector to be packaged.

28. (Three times amended) A producer cell line producing a retroviral particle, the producer cell comprising a retroviral vector and a DNA construct coding for proteins required for the retroviral vector to be packaged, said retroviral vector comprising in 5' to 3' order, a) a 5' long terminal repeat region of the structure U3-R-U5; b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the vector; and c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a heterologous promoter is inserted, wherein said promoter is other than a promoter from a retrovirus upon which the retroviral vector is based or a promoter from a subtype of the retrovirus upon which the retroviral vector is based and said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences.

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Please add new Claims 33-101 as follows:

33. (New) A retroviral vector which undergoes promoter conversion comprising in 5' to 3' order,

a) a 5' long terminal repeat region of the structure U3-R-U5;

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- b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the vector; and
- c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a promoter from a cellular gene is inserted, said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences.

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- 34. (New) The retroviral vector according to Claim 33, wherein said vector further comprises a regulatory element other than a promoter.
- 35. (New) The retroviral vector according to Claim 33, wherein said promoter is selected from the group consisting of: a Whey Acidic Protein promoter, β -lactoglobulin and casein specific promoters, a pancreas specific promoter, lymphocyte specific promoters, and combinations thereof.
- 36. (New) The retroviral vector according to Claim 33, wherein each long terminal repeat region is derived from a retrovirus selected from the group consisting of Murine Leukaemia Virus, Mouse Mammary Tumor Virus, Murine Sarcoma Virus, Simian Immunodeficiency Virus, Human Immunodeficiency Virus, Human T Cell Leukaemia Virus, Feline Immunodeficiency Virus, Feline Leukaemia Virus, Bovine Leukaemia Virus, Mason-Pfizer-Monkey Virus, and combinations thereof.
- 37. (New) The retroviral vector according to Claim 33, wherein said retroviral vector is derived from a BAG vector.
- 38. (Amended) The retroviral vector according to Claim 33, wherein the coding sequence is selected from the group consisting of marker genes, therapeutic genes, antiviral genes, antitumor genes, cytokine genes and combinations thereof.

39. (New) The retroviral vector according to Claim 38, wherein said marker or therapeutic gene is selected from the group consisting of β -galactosidase gene, neomycin gene, Herpes Simplex Virus thymidine kinase gene, puromycin gene, cytosine deaminase gene, hygromycin gene, secreted alkaline phosphatase gene, guanine phosphoribosyl transferase (gpt) gene, alcohol dehydrogenase gene, hypoxanthine phosphoribosyl transferase (HPRT) gene and combinations thereof.

40. (New) The retroviral vector according to Claim 33, wherein at least one of said coding sequences is a retroviral coding sequence that is an altered or at least partially deleted retroviral gene.

41. (New) The retroviral vector according to Claim 33, wherein retroviral sequences involved in integration of retroviruses are altered or at least partially deleted.

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42. (New) The retroviral vector according to Claim 33, wherein said promoter is regulatable by transacting molecules.

43. (New) A retroviral vector kit comprising:
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a retroviral vector which undergoes promoter conversion comprising in 5' to 3' order, a) a 5' long terminal repeat region of the structure U3-R-U5; b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the vector; and c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a promoter from a cellular gene is inserted, said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences; and
a packaging cell line harboring at least one retroviral or recombinant retroviral construct coding for proteins required for said retroviral vector to be packaged.

44. (New) The retroviral vector system according to Claim 43 wherein the packaging cell line harbors retroviral or recombinant retroviral constructs coding for those retroviral proteins which are not encoded in said retroviral vector.

45. (New) The retroviral vector system according to Claim 44 wherein the packaging cell line is selected from the group consisting of psi-2, psi-Crypt, psi-AM, GP+E-86, PA317, and GP+envAM-12.

46. (New) Recombinant retroviral particle obtained by transfecting a packaging cell line of a retroviral vector kit according to Claim 43 with the retroviral vector according to Claim 43, and culturing the cells under suitable conditions.

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47. (New) A retroviral provirus produced by infection of target cells with a recombinant retroviral particle according to Claim 46 whereby the promoter in the 3' long terminal repeat becomes duplicated during the process of reverse transcription in the target cell and appears in the 5' long terminal repeat as well as in the 3' long terminal repeat of the resulting provirus.

48. (New) mRNA of the retroviral provirus according to Claim 47.

49. (New) RNA of a retroviral vector according to Claim 33.

50. (New) Pharmaceutical composition containing a therapeutically effective amount of a recombinant retroviral particle according to Claim 46.

51. (New) A producer cell line producing a retroviral particle, the producer cell comprising a retroviral vector and a DNA construct coding for proteins required for the retroviral vector to be packaged, said retroviral vector comprising in 5' to 3' order, a) a 5' long terminal repeat region of the structure U3-R-U5; b) one or more sequences selected from

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coding and non-coding sequences, said sequences being inserted into the body of the vector; and c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a promoter from a cellular gene is inserted, said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences.

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52. (New) A method for introducing homologous or heterologous nucleotide sequences into cells in an animal or cultured cells, said method comprising infecting the cells with recombinant retroviruses produced by the producer cell line of Claim 51.

53. (New) The method according to Claim 52, wherein the nucleotide sequences are selected from the group consisting of genes or parts of genes encoding for proteins, regulatory sequences and promoters and combinations thereof.

54. (New) A recombinant retroviral particle comprising the retroviral vector according to Claim 33.

55. (New) The retroviral vector according to Claim 33, wherein said promoter is target cell specific in its expression.

56. (New) A retroviral vector which undergoes promoter conversion comprising in 5' to 3' order,

- a 5' long terminal repeat region of the structure U3-R-U5;
- one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the vector; and
- Sub H7* c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a heterologous retroviral promoter which is derived from a promoter of a retrovirus other than a retrovirus upon which the retroviral vector is based or other than a

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subtype of the retrovirus upon which the retroviral vector is based is inserted, said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences.

57. (New) The retroviral vector according to Claim 56, wherein said vector further comprises a regulatory element other than a promoter.

58. (New) The retroviral vector according to Claim 56, wherein said promoter is selected from the group consisting of a Mouse mammary Tumor specific promoter, a Mouse Mammary Tumor Virus specific promoter conferring responsiveness to glucocorticoid hormones or directing expression to the mammary gland, and combinations thereof.

59. (New) The retroviral vector according to Claim 56, wherein each long terminal repeat region is derived from a retrovirus selected from the group consisting of Murine Leukaemia Virus, Mouse Mammary Tumor Virus, Murine Sarcoma Virus, Simian Immunodeficiency Virus, Human Immunodeficiency Virus, Human T Cell Leukaemia Virus, Feline Immunodeficiency Virus, Feline Leukaemia Virus, Bovine Leukaemia Virus, Mason-Pfizer-Monkey Virus, and combinations thereof.

60. (New) The retroviral vector according to Claim 56, wherein said retroviral vector is derived from a BAG vector.

61. (Amended) The retroviral vector according to Claim 56, wherein the coding sequence is selected from the group consisting of marker genes, therapeutic genes, antiviral genes, antitumor genes, cytokine genes and combinations thereof.

62. (New) The retroviral vector according to Claim 61, wherein said marker or therapeutic gene is selected from the group consisting of β -galactosidase gene, neomycin gene, Herpes Simplex Virus thymidine kinase gene, puromycin gene, cytosine deaminase gene, hygromycin gene, secreted alkaline phosphatase gene, guanine phosphoribosyl transferase

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(gpt) gene, alcohol dehydrogenase gene, hypoxanthine phosphoribosyl transferase (HPRT) gene and combinations thereof.

63. (New) The retroviral vector according to Claim 56, wherein at least one of said coding sequences is a retroviral coding sequence that is an altered or at least partially deleted retroviral gene.
64. (New) The retroviral vector according to Claim 56, wherein retroviral sequences involved in integration of retroviruses are altered or at least partially deleted.
65. (New) The retroviral vector according to Claim 56, wherein said promoter is regulatable by transacting molecules.

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66. (New) A retroviral vector kit comprising:

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a retroviral vector which undergoes promoter conversion comprising in 5' to 3' order, a) a 5' long terminal repeat region of the structure U3-R-U5; b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the vector; and c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a heterologous retroviral promoter other than a promoter from a retrovirus upon which the retroviral vector is based or other than a subtype of the retrovirus upon which the retroviral vector is based is inserted, said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences; and

a packaging cell line harboring at least one retroviral or recombinant retroviral construct coding for proteins required for said retroviral vector to be packaged.

67. (New) The retroviral vector system according to Claim 66 wherein the packaging cell line harbors retroviral or recombinant retroviral constructs coding for those retroviral proteins which are not encoded in said retroviral vector.

68. (New) The retroviral vector system according to Claim 66 wherein the packaging cell line is selected from the group consisting of psi-2, psi-Crypt, psi-AM, GP+E-86, PA317, and GP+envAM-12.

69. (New) Recombinant retroviral particle obtained by transfecting a packaging cell line of a retroviral vector kit according to Claim 66 with the retroviral vector according to Claim 66, and culturing the cells under suitable conditions.

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70. (New) A retroviral provirus produced by infection of target cells with a recombinant retroviral particle according to Claim 69 whereby the promoter in the 3' long terminal repeat becomes duplicated during the process of reverse transcription in the target cell and appears in the 5' long terminal repeat as well as in the 3' long terminal repeat of the resulting provirus.

71. (New) mRNA of the retroviral provirus according to Claim 70.

72. (New) RNA of a retroviral vector according to Claim 56.

73. (New) Pharmaceutical composition containing a therapeutically effective amount of a recombinant retroviral particle according to Claim 69.

74. (New) A producer cell line producing a retroviral particle, the producer cell comprising a retroviral vector and a DNA construct coding for proteins required for the retroviral vector to be packaged, said retroviral vector comprising in 5' to 3' order, a) a 5' long terminal repeat region of the structure U3-R-U5; b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the

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vector; and c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a heterologous retroviral promoter other than a promoter from a retrovirus upon which the retroviral vector is based or other than a subtype of the retrovirus upon which the retroviral vector is based is inserted, said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences.

75. (New) A method for introducing homologous or heterologous nucleotide sequences into cells in an animal or cultured cells, said method comprising infecting the cells with recombinant retroviruses produced by the producer cell line of Claim 74.

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76. (New) The method according to Claim 75, wherein the nucleotide sequences are selected from the group consisting of genes or parts of genes encoding for proteins, regulatory sequences and promoters and combinations thereof.

77. (New) A recombinant retroviral particle comprising the retroviral vector according to Claim 56.

78. (New) The retroviral vector according to Claim 56, wherein said promoter is target cell specific in its expression.

79. (New) A retroviral vector which undergoes promoter conversion comprising in 5' to 3' order,

a) a 5' long terminal repeat region of the structure U3-R-U5;

b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the vector; and

c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a heterologous promoter other than a retroviral promoter is inserted, said promoter

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regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences.

80. (New) The retroviral vector according to Claim 79, wherein said vector further comprises a regulatory element other than a promoter.

81. (New) The retroviral vector according to Claim 79, wherein said promoter is selected from the group consisting of: a Whey Acidic Protein promoter, β -lactoglobulin and casein specific promoters, a pancreas specific promoter, lymphocyte specific promoters, and combinations thereof.

82. (New) The retroviral vector according to Claim 79, wherein each long terminal repeat region is derived from a retrovirus selected from the group consisting of Murine Leukaemia Virus, Mouse Mammary Tumor Virus, Murine Sarcoma Virus, Simian Immunodeficiency Virus, Human Immunodeficiency Virus, Human T Cell Leukaemia Virus, Feline Immunodeficiency Virus, Feline Leukaemia Virus, Bovine Leukaemia Virus, Mason-Pfizer-Monkey Virus, and combinations thereof.

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83. (New) The retroviral vector according to Claim 79, wherein said retroviral vector is derived from a BAG vector.

84. (Amended) The retroviral vector according to Claim 79, wherein the coding sequence is selected from the group consisting of marker genes, therapeutic genes, antiviral genes, antitumor genes, cytokine genes and combinations thereof.

85. (New) The retroviral vector according to Claim 84, wherein said marker or therapeutic gene is selected from the group consisting of β -galactosidase gene, neomycin gene, Herpes Simplex Virus thymidine kinase gene, puromycin gene, cytosine deaminase gene, hygromycin gene, secreted alkaline phosphatase gene, guanine phosphoribosyl transferase

(gpt) gene, alcohol dehydrogenase gene, hypoxanthine phosphoribosyl transferase (HPRT) gene and combinations thereof.

86. (New) The retroviral vector according to Claim 79, wherein at least one of said coding sequences is a retroviral coding sequence that is an altered or at least partially deleted retroviral gene.

87. (New) The retroviral vector according to Claim 79, wherein retroviral sequences involved in integration of retroviruses are altered or at least partially deleted.

88. (New) The retroviral vector according to Claim 79, wherein said promoter is regulatable by transacting molecules.

89. (New) A retroviral vector kit comprising:

a retroviral vector which undergoes promoter conversion comprising in 5' to 3' order, a) a 5' long terminal repeat region of the structure U3-R-U5; b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the vector; and c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a heterologous promoter other than a retroviral promoter is inserted, said promoter regulating, after infection of a target cell, expression of said one or more sequences selected from coding and non-coding sequences; and

a packaging cell line harboring at least one retroviral or recombinant retroviral construct coding for proteins required for said retroviral vector to be packaged.

90. (New) The retroviral vector system according to Claim 89 wherein the packaging cell line harbors retroviral or recombinant retroviral constructs coding for those retroviral proteins which are not encoded in said retroviral vector.

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91. (New) The retroviral vector system according to Claim 89 wherein the packaging cell line is selected from the group consisting of psi-2, psi-Crypt, psi-AM, GP+E-86, PA317, and GP+envAM-12.

92. (New) Recombinant retroviral particle obtained by transfecting a packaging cell line of a retroviral vector kit according to Claim 89 with the retroviral vector according to Claim 89, and culturing the cells under suitable conditions.

93. (New) A retroviral provirus produced by infection of target cells with a recombinant retroviral particle according to Claim 92 whereby the promoter in the 3' long terminal repeat becomes duplicated during the process of reverse transcription in the target cell and appears in the 5' long terminal repeat as well as in the 3' long terminal repeat of the resulting provirus.

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94. (New) mRNA of the retroviral provirus according to Claim 93.

95. (New) RNA of a retroviral vector according to Claim 79.

96. (New) Pharmaceutical composition containing a therapeutically effective amount of a recombinant retroviral particle according to Claim 92.

97. (New) A producer cell line producing a retroviral particle, the producer cell comprising a retroviral vector and a DNA construct coding for proteins required for the retroviral vector to be packaged, said retroviral vector comprising in 5' to 3' order, a) a 5' long terminal repeat region of the structure U3-R-U5; b) one or more sequences selected from coding and non-coding sequences, said sequences being inserted into the body of the vector; and c) a 3' long terminal repeat region comprising a partially deleted U3 region wherein in said partially deleted U3 region a polylinker sequence containing a heterologous promoter other than a retroviral promoter is inserted, said promoter

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